National Institute of Allergy and Infectious Diseases

Council News

September 1998 Council *Vol. 7 No. 3*

Balancing the Budget in FY 1999

As we noted in our last newsletter issue, NIAID will pay unsolicited grant applications to the 20.0 percentile as part of the Institute's FY 1999 financial management plan (see the table on page 15).

The decision to lower the payline to the 20.0 percentile was made after considerable discussion in NIAID and with Council.

Because this year's payline is lower than the FY 1998 payline for unsolicited grants, this change has created some concerns in the scientific community.

A percentile payline implies a percentage of grants to be funded. Thus, lowering the percentile may suggest that the percentage of grants funded will be reduced.

However, this is not correct because, even at the lower percentile funding level of 20.0, NIAID is projecting to fund more competitive grants than we did last year.

Why then is there this apparent contradiction? The reasons are complex. The full article on our web site attempts to put all factors into a logical context and answer questions we have received regarding some of our key budgetary

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New Address for NIAID *Council News* Web Site

Update your bookmark!

Due to technical changes, we have a new Internet address:

http://www.niaid.nih.gov/ncn

To help readers adjust, we are redirecting traffic to the new address from the old one for the next few months.

The extramural information center is now the third most frequented site on the NIAID home page!

Thank you for bearing with us during this latest transition.

Inside

INITIATIVES & funding

NIAID Restructures and Expands HIV Vaccine Program

As part of a redesigned vaccine program, NIAID's Division of AIDS (DAIDS) is launching new initiatives for vaccine and other prevention research and creating resources to help investigators advance ideas and vaccine designs at every stage.

With inflows of monies building the research base, NIAID is expanding research opportunities at all stages of the pipeline. For example, two new preclinical support contracts will help investigators realize their ideas at virtually any step along the R&D continuum.

Further, a restructured clinical program strengthens links between basic researchers and relevant clinical samples by making basic research an integrated part of the scientific agenda of the new network.

"The revitalization began with the work of the Baltimore committee, which bolstered research at the front end. The new programs make sure we get results from those efforts," noted Dr. Margaret Johnston, head of NIAID's HIV vaccine research effort (see Staff article on page 7).

Dr. Johnston added that the new programs let basic researchers move beyond their realms and participate in moving their vaccine designs into clinical research.

Aimed to please both academia and the private sector, NIAID's overlapping programs will bolster research of all types of HIV prevention strategies, from vaccines to microbicides and other approaches to preventing sexual and maternal-infant transmission.

Two HIV trial networks

Two RFAs are already soliciting applications for two separate networks to spearhead HIV vaccine and other prevention trials here and abroad: the HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN).

Replacing the HIV Network for Prevention Trials (HIVNET) and AIDS Vaccine Evaluation Group, the new networks will be headed by leadership groups charged with identifying, prioritizing, and conducting the studies.

In May, NIAID will publish two additional RFAs soliciting applications for the research units that will bring additional scientific talent to conduct the trials.

The network will have the capability to conduct all phases of clinical research. For the HVTN, NIAID is allocating about $12 million to the central group and another approximately $13

NIAID Vaccine Initiatives

HIV Prevention Trials Network Leadership Group

http://www.nih.gov/grants/guide/rfa-files/RFA-AI-98-015.html

HIV Vaccine Trials Network Leadership Group

http://www.nih.gov/grants/guide/rfa-files/RFA-AI-98-015.html

HIV Vaccine Research and Design

Integrated Preclinical/Clinical AIDS Vaccine Development

HIV Vaccine Production

http://www.niaid.nih.gov/contract/rfp's/rfp9921.htm

HIV Vaccine Design and Development Teams

RFP to be released in FY 1999

Innovation Grants

million (in first-year support) for the research units; for the HPTN, those figures are about $8 million and $10 million, respectively.

The prevention group will focus on such nonvaccine modalities as antiretrovirals, microbicides, behavioral approaches, barrier methods, immunologic strategies, STD treatments, and others; studies will include perinatal HIV transmission.

Both efforts will be headed by leadership groups that will provide scientific leadership and coordination. You can find the RFAs in the *NIH Guide* (see box on page 2).

With our mandate to include basic research that can be addressed through vaccine trials, NIAID is expanding opportunities for collaborations on basic science questions, such as the study of viral and host factors related to transmission and prevention.

By helping to define the scientific agenda, basic scientists can ensure at the outset that appropriate samples are collected during the study.

New support contracts

NIAID's two new contract programs, HIV Vaccine Production and HIV Vaccine Design and Development Teams, will provide expertise and resources to companies and academic investigators to move a product to phase I or II clinical trial. The HIV

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New Vaccine Contract: HIV Vaccine Production

Provides resources to help move an HIV vaccine idea from the lab to clinical testing.

Three main functions are scale-up and production, safety and immunogenicity testing in animals, and preparation for FDA submissions.

Multiple awards for up to seven years will start in August 1999.

New Contract: HIV Vaccine Design and Development Teams

Contract funds consortia of scientists from academia or industry who have promising vaccine ideas and a vaccine design suitable for development.

Teams will advance the product along a defined development path with the contract providing resources and personnel.

Investigators can have products at any stage of development including those ready for clinical studies up to phase II.

Multiple awards for up to five years will start in September 1999.

Existing grant programs for all stages of vaccine research and development

Innovation Grant Program

Novel, innovative, or high-risk projects reflecting innovative vaccine discovery and development ideas.

HIV Research and Design Program (HIVRAD)

Basic, including animal, studies developed beyond the initial idea stage.

Integrated Preclinical/Clinical Program (IPCAVD)

Research projects ready to begin preliminary studies in people during the grant period.

NIH Is Looking for Bioengineering Applications and Partnerships

On October 29, NIH published two program announcements (PA) soliciting grants for bioengineering research.

One PA seeks grant applications in that field, and the other fosters multidisciplinary collaborations, bringing together teams of bioengineering and basic or clinical investigators. Most NIH institutes and centers, including NIAID, are participating in the PAs.

Find the Bioengineering Research Grants PA on the web at **http://www.nih.gov/grants/guide/pa-files/PAR-99-009.html**.

The Bioengineering Research Partnerships PA is online at **http://www.nih.gov/grants/guide/pa-files/PAS-99-010.html**.

Some NIAID PAs Are No Longer in Effect

In October, NIAID inactivated the 18 program announcements listed below.

Please be aware that, although you can still access these PAs in the *NIH Guide* web site, they have been retired, and the Institute will not accord them the special funding consideration given to our active PAs. To find NIAID's active program announcements, go to **http://www.niaid.nih.gov/ncn/pa-table.htm** in the Initiative section of the *Council News* web site at **http://www.niaid.nih.gov/ncn/in-main.htm**.

Inactive NIAID Program Announcements*

PA-96-048 Expanded Research on Emerging Diseases, May 3, 1996
PA-96-051 Role of Microbes in Autoimmunity/Immune-Mediated Diseases, May 10, 1996
PA-96-053 Gender in the Pathogenesis of Autoimmunity, May 10, 1996
PA-97-003 The Immunobiological Consequences of Aging, October 18, 1996
PA-97-073 Mucosal Immunity in the Pathogenesis/Prevention of Human Disease, July 18, 1997
PA-97-075 Direct versus Indirect Antigen Recognition in Allograft Survival, July 25, 1997
PA-97-076 The Immunobiological Aspects of Hematopoietic Stem Cells, July 25, 1997
PA-97-077 Minor Histocompatibility Antigens in GVHD and Graft Rejection, July 25, 1997
PA-97-078 Inflammation in Asthma and Allergy, July 25, 1997
PA-97-079 Innate Immunity, July 25, 1997
PA-97-081 Basic and Clinical Research on Immune Tolerance, July 25, 1997
PA-97-089 Mechanisms of Immune Response to Xenotransplantation Antigens, August 8, 1997
PA-97-090 Three-Dimensional Structures of Immunological Proteins, August 8, 1997
PA-97-098 Autoimmunity: Genetics, Mechanisms and Signaling, August 29, 1997
PA-97-099 Genes and Mechanisms Underlying Primary Immunodeficiency, August 29, 1997
PA-97-100 Regulation of the Immune Response, August 29, 1997
PA-97-101 Basic Mechanisms of Vaccine Efficacy, August 29, 1997
PA-98-013 Generation and Maintenance of Immunological Memory, December 5, 1997

*date is the *NIH Guide* announcement

NIH news

NIH Adopts Modular Grants

In October, Dr. Varmus approved the use of modular grants for applications targeting the June 1, 1999, receipt date.

Rather than preparing detailed budgets, applicants will request funds for direct costs in increments of $25,000, up to $250,000.

Another big difference from the traditional grant is that modular grants will not receive annual budget increases, a factor applicants will need to take into account when preparing a budget request. The number of modules requested can vary from year to year.

NIH will use the approach for research project grants (R01), small grants (R03), academic research enhancement awards (R15), and exploratory or developmental grants (R21), whether the application is investigator initiated or responding to a program announcement or request for applications.

Small Business Innovation Research phase I (R41) and Small Business Technology Transfer phase I (R43) applications will go the modular route beginning April 15.

Read more in the online *Guide* announcement at **http://www.nih.gov/grants/guide/notice-files/not98-178.html**.

Grantees Can Opt for an Electronic Notification of Grant Award

After a successful pilot showed the feasibility of the approach, NIH is giving grantee institutions the option of getting a notice of grant award electronically.

Institutions must register with NIH and should establish a single email address specifically for this purpose.

All information in the paper NGA will be in the E-NGA. Institutions will continue to be responsible for distributing E-NGAs and any special terms and conditions to the principal investigator and other appropriate persons.

Though the E-NGA is currently an option, it will be obligatory at some point in the future. See the September 16 *Guide* announcement at **http://www.nih.gov/grants/guide/notice-files/not98-129.html** for details.

Use New Grant Application Forms

NIH recently updated the forms and instructions for new grant applications (PHS 398) and continuing grant applications (PHS 2590), both dated April 1998.

They *must* be used for the May 10, 1999, and later receipt dates.

Both forms are on the web at **http://www.nih.gov/grants/forms.htm**.

NIH prefers that you download the forms from the Internet; however, you can request printed copies from:

Grants Information
Division of Extramural Outreach and Information Resources
National Institutes of Health
6701 Rockledge Drive, Suite 6095
Bethesda, MD 20892-7910
Telephone: 301/435-0714
Email: GrantsInfo@nih.gov

Forms for Individual National Research Service Awards (PHS 416-1 and PHS 416-9) are also being revised.

Major changes to PHS 398

These are the key changes:

- New investigator check box on the face page.

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New Application Forms—

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- Social security number (item 3c on the face page) shaded out (social security number goes on form page KK only).
- Inclusion of children in research in the research plan.
- Additional instructions for submitting proprietary information.
- Just-in-time requirements for research career awards and table of contents (form page LL). Other support information for sponsors and cosponsors now on page 7-GG.
- 25-page limit on research career awards for candidate, item 3, and research plan, item 6 a.-d.
- Phone number for express mail and courier service delivery on label page.

Key changes to PHS 2590

- More detailed instructions for the Streamlined Noncompeting Award Process (SNAP).
- Inclusion of children in research in the progress report summary.

Please note the following error in the printed version: in the biographical sketch, form page FF, the last line of instructions should state "Do not exceed two pages." The Acrobat version on the NIH web site is correct.

See Our List of NIAID's Top 100 Institutions on the Web

At the request of several grantees, we have placed a list of the top 100 institutions supported by NIAID on the web.

This information lets investigators see how their institutions are faring and helps trainees find training programs. Ranked by level of support, the list shows research, contract, fellowship, and training dollars for each institution.

Find it at **http://www.niaid.nih.gov/ncn/pdf/ranking.pdf.** You can also get there via the Toolbox section of the *Council News* web site under the More Tools header.

To view our Acrobat files, be sure to use **Acrobat Reader 3.0**, which you can download free at **http://www.adobe.com/prodindex/acrobat readstep.html**. Earlier versions will ***not*** work.

Model SBIR Application Is Online

Looking for help writing an SBIR application?

You can find an example of an outstanding SBIR application on the web at **http://www.nhlbi.nih.gov/nhlbi/sbir/modelsbi.htm**.

Posted by the National Heart, Lung, and Blood Institute, the content is from a phase I application that progressed successfully to phase II.

You can also get there from our link from the *Council News* web site's Toolbox at **http://www.niaid.nih.gov/ncn/toolmain.htm**. Look under the Research Grants header.

NRSA Stipends Go Up 25 Percent

Stipends for National Research Service Award training grants and fellowships are rising 25 percent this fiscal year.

See the *Guide* announcement at **http://www.nih.gov/grants/guide/notice-files/not98-161.html** for details.

PI Salary Caps Edge Up a Notch

PI salary limits are going up by $900.

The maximum amount a PI can be paid on an NIH grant has increased from $125,000 to $125,900.

This level corresponds to the executive level II salary of senior federal employees.

INSTITUTE&staff

Staff Changes

At Council, Dr. Fauci announced several staff changes. As we reported in our last issue, Dr. Peggy Johnston returned to NIAID as assistant director for HIV/AIDS vaccines and associate director of the Vaccine and Prevention Research Program in the Division of AIDS.

Dr. Fauci commented, "Her experience and understanding of the international community in AIDS vaccine development will be of enormous benefit, particularly as we open the first overseas phase I trial in Uganda this year. We are very pleased to have Peggy back."

In the Division of Microbiology and Infectious Diseases (DMID), Dr. Regina Rabinovich was recently appointed chief of the Clinical and Regulatory Affairs Branch.

For the past four years, she has managed the Vaccine and Treatment Evaluation Units, which conduct studies of candidate vaccines at universities across the U.S.

Dr. Rabinovich also represents NIH at the Advisory Commission on Immunization Practices, the Redbook Committee of the American

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Dr. Matthew Waldor Gets Prestigious Presidential Award

NIAID grantee Dr. Matthew Waldor is the worthy recipient of the 1998 Presidential Early Career Award for Scientists and Engineers. Given to the nation's most promising young scientists and engineers, this prestigious kudo was awarded to Dr. Waldor for "the most significant discovery in cholera pathogenesis research in decades."

Dr. Waldor received both his M.D. and Ph.D. in immunology from Stanford University, studying for the latter under Dr. Lawrence Steinman. His interest in cholera vaccines began during his postdoctoral training under Dr. John Mekalanos at Harvard Medical School.

While a postdoc, Dr. Waldor, together with Dr. Mekalanos, showed how a nontoxic strain of *Vibrio cholerae* can become pathogenic by acquiring toxin genes from a novel filamentous bacteriophage, CTX.

Cholera toxin is encoded in the genome of CTX, the first phage of its kind shown to encode a bacterial virulence factor.

From these studies emerges a mechanism for the transfer of bacterial virulence genes with implications for vaccines using live organisms.

For full virulence, *V. cholerae* needs coordinated regulation by the expression of two critical virulence factors: the enterotoxin cholera toxin (CT), which causes life-threatening diarrhea, and toxin-coregulated pili (TCP), surface organelles that enable colonization of the bacteria.

With his laboratory colleagues, Dr. Waldor, now an assistant professor at the New England Medical Center and Tufts University School of Medicine, discovered the CTX receptor and the TCP pilus and showed how CTX infects

The studies suggest gene exchange occurs in the host, raising the possibility that host-derived signals regulate gene transfer among pathogens.

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Dr. Waldor—*continued from page 7*

ctxAB⁻ V. cholerae strains in the intestinal tracts of mice via TCP. Benign cholera bacteria can then become deadly by acquiring packages of CT genes from CTX.

In their murine model, the scientists saw that intestinal infection of *ctxAB⁻ V. cholerae* strains is extremely efficient, suggesting that gene exchange takes place in the host and raising the possibility that host-derived signals help regulate gene transfer among pathogens.

Dr. Waldor also determined that the phage can infect live-attenuated vaccine strains, resulting in vaccine reversion to toxinogenicity, which highlights a potential biosafety limitation of current live cholera vaccines.

However, his group also found that the CTX repressor protein can render a phage-susceptible vaccine strain immune to infection, a promising finding that may address this safety issue.

Future and ongoing studies in Dr. Waldor's lab are exploring the molecular biology of this novel bacteriophage.

New Research Resource: NIAID Tetramer Facility

NIAID is establishing a facility to synthesize and distribute standardized, tetrameric, soluble MHC class I peptide reagents for analyzing antigen-specific CD8+ T cells.

Planned to open in early 1999, the facility is supported by all NIAID divisions through a contract housed in the AIDS Research and Reference Reagent Program.

Investigators seeking to use this resource will request approval from NIAID program staff, who will review requests for scientific merit.

Successful investigators will provide purified peptide and pay for shipping costs. The facility will provide enough tetramer staining reagent to analyze 250 to 500 specimens.

When the system is up and running, we will publish guidelines for requesting tetramers on the NIAID home page.

STEC Reference Center Funded by NIAID

NIAID is sponsoring a repository for strains and data relevant to Shiga toxin-producing *Escherichia coli* (STEC).

Headed by Dr. Thomas Whittam, the STEC Strain Collection and Reference Center at Pennsylvania State University houses a standard reference collection of well-characterized STEC strains and a central online database.

The center serves as a repository for strains isolated from new outbreaks and environments and will conduct rapid characterization of included STEC strains based on genetic markers of clonal identity and virulence genes.

Strains will be subtyped by sequencing flagellin and toxin genes. Further, the center maintains an online database integrating new data from collaborating researchers.

Overseeing the quality of the effort, an advisory committee will determine which strains to include, recommend tests to characterize the strains, and ensure the quality of submitted data.

Collecting complete data sets on these standard strains should allow a more rapid comparison of strains and help identify bacterial factors associated with *in vitro* assay results, pathogenesis in animal models, and clinical outcomes.

NIAID expects to include strains from human outbreaks and sporadic cases as well as

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New Rotavirus Vaccine—Fruition of Research Investment, Wins NIAID Investigator Prestigious Award

Two decades of work by NIAID labs and grantees have led to FDA approval of the first vaccine for rotavirus, the most common cause of severe diarrhea in children.

In a highly collaborative effort, the quadrivalent vaccine was tested in nearly 18,000 people in the U.S. and abroad.

About 80 percent of children in the U.S. suffer from rotavirus, which causes about 900,000 deaths annually, mostly in developing countries.

Called Rotashield,™ the vaccine is the culmination of long and devoted work by scientists in the Laboratory of Infectious Diseases (LID), spearheaded by Albert Z. Kapikian, M.D., head of the Epidemiology Section, and Robert Chanock, M.D., LID chief.

LID scientists have been studying gastroenteritis since the late 1960s.

Using electron microscopy, Dr. Kapikian discovered Norwalk virus, the first virus associated with gastroenteritis, in 1972. This finding led to the discovery of rotavirus by Australian scientists the following year.

The LID investigators have also been intimately involved with clinical trials of vaccine candidates, developing a monovalent rotavirus vaccine in 1984. Two years later, they developed the additional components of the vaccine after realizing that a monovalent product might not protect against the four main clinical strains of rotavirus.

On August 31, FDA licensed the orally administered Rotashield,™ to Wyeth-Ayerst Laboratories for use in children at ages 2, 4, and 6 months.

For more information, see the FDA news release at **http://www.fda.gov/bbs/topics/NEWS/NEW00652.html**.

Commercial development began in 1987 through a cooperative research and development agreement with Wyeth-Ayerst.

About 80 percent of children in the U.S. suffer from rotavirus infection; worldwide, the organism causes about 900,000 deaths annually, mostly in developing countries.

Dr. Albert Kapikian Gets CVI Pasteur Award

Together with two other scientists, Dr. Kapikian received the 1998 Children's Vaccine Initiative (CVI) Pasteur Award for Recent Contributions to Vaccine Development in November.

The investigators were cited collectively for "outstanding work contributing to the development of rotavirus vaccines and their future utilization."

For more information, read the NIAID press release at **http://www.niaid.nih.gov/newsroom/kapikian.htm**.

STEC Reference Center—*continued from page 8*

animal and environmental isolates representing several serotypes.

Find the STEC Reference Center on the web at **http://www.bio.psu.edu/faculty/whittam/STEC/.** For more information, call NIAID's Dr. Dennis Lang, 301/496-7051, or send him email to **dl73v@nih.gov**.

Foodborne Pathogens: How Little We Know

America is facing a growing threat from foodborne pathogens, Dr. Michael Osterholm told Council in September, and we know less about the problem today than we did 50 years ago.

Dr. Osterholm's research team was one of the first to call attention to the changing epidemiology of foodborne disease. He is state epidemiologist and chief of the Acute Disease Epidemiology Section at the Minnesota Department of Health.

"The organisms are there, we're just not finding them. This is the part of the iceberg that's unrecognized, the other 98 percent."

Scope of the problem unknown

Dr. Osterholm's studies in Minnesota show that people average 1.8 such illnesses each year.

Campylobacter is by far the state's number one bacterial pathogen, with *Salmonella*, *E. coli, Shigella, Yersinia, Listeria*, and others accounting for more than 6 million reported cases.

Rates have shot up dramatically from historical norms of about one instance per year, and no one knows why.

Diarrhea and abdominal pain are the number one reason for emergency room visits in this country; however, it is unclear how much of it is foodborne disease. Not all foodborne illness is diarrhea and vomiting, and those symptoms do not always stem from infected foods.

A key obstacle to sizing up the problem is that our surveillance system does an inadequate job of picking up these illnesses, and full-blown outbreaks are minor in proportion to continuing instances of infection.

"Surveillance for outbreaks of sporadic cases is picking up a very, very small piece of what's happening out there," noted Dr. Osterholm.

He gave a striking example of our failure to comprehend what is occurring in our communities.

This summer, his group traced a Minnesota outbreak of first *Shigella* and then enterotoxigenic *E. coli* to the same parsley fields in Mexico.

Although this was a serious polymicrobial outbreak, no other organizations picked it up until contacted by Dr. Osterholm and his group.

After this prompting, the outbreak was then discovered from California to Florida and Canada.

"This is the part of the iceberg that's unrecognized, the other 98 percent of what's out there. The organisms are there, we're just not finding them," he asserted.

In general, less than 2 percent of diarrheal episodes are attributed to classic foodborne agents.

But many organisms have yet to be discovered. For example, just during the last year, Dr. Osterholm's group discovered three different kinds of enterotoxigenic *E. coli* that do not fit the classic characteristics of diarrheal *E. coli*.

Why the problem is growing

As our food habits evolve, Americans are exposed to more and new organisms. Our food sources are increasingly international, much of it grown, harvested, and handled in ways prone to spread disease.

One vector is people. Half of the American food dollar is spent outside the home for food prepared by people who may have minimal edu-

cation and a high prevalence of intestinal parasites.

Then there are salad bars. "What the food-handler or Mother Nature haven't done to it, the customer will; then you keep that food at the wrong temperature, and salad bars are probably the worst kind of food safety situation imaginable," attested Dr. Osterholm.

> ***"We have a whole world of pathogens out there to discover."***

Animals provide another route. For example, *E. coli* O157:H7 has infected birds, whose droppings can contaminate our food.

Further, new methods of mass food production can spread germs throughout facilities producing millions of tons of foodstuffs.

Also, as the population ages, more people become high risk.

In Minnesota, 125,000 people are now living with cancer; this figure rises to about 350,000 in 15 years, with serious implications for the outcomes of foodborne disease.

Worldwide grocery store

In America the typical grocery has 60,000 food items, with 15,000 new items competing for shelf space every year.

More often, produce originates in the developing world because we can chase the sun around the world at an economical cost.

"When people tell us we have the safest food supply in the world, my response is we have the world's food supply," said Dr. Osterholm.

Nearly impossible to disinfect, produce is a major culprit.

In Minnesota, 30 percent of foodborne disease cases where a vehicle is identified are traced to fresh produce.

Raspberries, for example, have hairy follicles capable of housing agents even after scrubbing.

The stomata of a lettuce leaf hide *E. coli* O157:H7. Some agents, including *Salmonella*, can adhere to the pistil of a tomato plant and become incorporated into the meat of the tomato.

Dr. Osterholm felt that we must find a way to pasteurize our produce. "We have some real challenges," he stated, "irradiation is a possible solution."

In addition to *E. coli* O157:H7, other animal pathogens will likely make new encounters with our GI tracks.

In 1996, after chloroquinoline was approved for use in poultry to counter respiratory infections, Dr. Osterholm found that 80 percent of chickens sampled in Minnesota were flooded with *Campylobacter*, creating a huge reservoir of chloroquinoline-resistant organisms.

Chloroquinoline was recently approved for use in red meat.

He also recently found 35 enteric pathogens in animals that have not previously been identified in people.

Next horizon

Researchers need to determine which diseases are foodborne and which infections stem from another mechanism.

> ***"Some agents, including* Salmonella*, can adhere to the pistil of a tomato plant and become incorporated into the meat of the tomato."***

We must also define the agents, where they come from, and how we interface with them.

"These are areas for NIH to consider, where NIH could be very helpful," he advised, "I guarantee we're going to find a lot more foodborne disease than we ever thought was foodborne disease. We have a whole world of pathogens out there to discover."

Experts Help Shape Tolerance Research Plan

Director of the Division of Allergy, Immunology, and Transplantation (DAIT) Dr. Daniel Rotrosen presented Council with NIAID's research tolerance plan, developed with input from panels of representatives from the research community, interest groups, and industry.

Panelists recommended a mechanism- rather than disease-based approach of basic, exploratory, and developmental research, including work in nonhuman primates.

Relying on both solicited and unsolicited research, studies must explore transplantation, asthma, allergy, and autoimmune diseases, including the development of markers showing early induction, maintenance, and loss of tolerance.

Following the group's advice, NIAID is already working closely with industry on ideas for new projects.

Find the tolerance plan at **http://www.niaid.nih.gov/publications/immune/bookcover.htm**.

To set the stage for a tolerance network, NIAID published an RFP in November, Collaborative Network for Clinical Research on Immune Tolerance.

A single contract will integrate four components into a collaborative network. Co-sponsored with Juvenile Diabetes Foundation International (JDFI), it will focus on kidney and islet transplantation, asthma and allergy, and autoimmune diseases.

Find the RFP on the web at **http://www.niaid.nih.gov/publications/immune/rfp1.htm.**

As part of this effort, a consortium of institutions will accelerate research to:

- treat immune-mediated diseases
- conduct clinical trials
- study mechanisms of tolerance induction and loss as part of the trials
- develop assays of tolerance induction and loss

Early on, NIAID sent an email message to 1,000 NIH investigators announcing the draft solicitation.

And before finalizing the RFP, NIAID heard investigators' ideas during a unique online comment period between September 21 and October 14.

Besides letting people air views, it also enabled NIAID to assess whether investigators were interested in applying and helped scientists to see who may want to collaborate with them.

Hundreds of people showed interest, including major players in the field. The RFP was published in November; an award will be made at the end of the fiscal year.

In addition to the RFP, NIAID is jump-starting its

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Capsule of Recommendations by Two Expert Panels

Create a network of basic and clinical investigators and programs.

Foster multi-institutional and multisector partnerships and approaches.

Ensure scientific and administrative flexibility.

Study underlying mechanisms in nonhuman primates and in people.

Support basic research to expand knowledge of the molecular basis of tolerance.

Focus on the most appropriate approaches for clinical trials.

Incorporate developmental work to identify and validate surrogate markers.

Ensure adequate research resources, including training investigators.

Staff News—*continued from page 7*

Academy of Pediatrics, and the National Vaccine Advisory Committee.

Ms. Brenda J. Velez is the new chief of the Contract Management Branch in the Division of Extramural Activities, where she oversees the Institute's research contract activities.

Ms. Velez has held various contract positions in NIAID since 1986, including that of chief of the AIDS Clinical Research Contract Section.

Dr. Jane Kinsel is the new director of the Office of Policy Analysis (OPA) in the Office of the NIAID Director, replacing Ms. Sarah Carr.

Dr. Kinsel was associate director, DMID, and has been acting head of OPA since June.

Tolerance Research Plan—*continued from page 12*

new efforts with NIH funds to support three unsolicited P01s in basic mechanisms of tolerance induction and kidney transplantation in nonhuman primates.

We are also cosponsoring a phase I clinical trial with biotech company Biogen, Inc., that will begin shortly, and we are supplementing three NIAID grants to study the mechanisms of kidney graft maintenance in clinical trials.

NIAID Expert Panel on Immune Tolerance

Abul Abbas, M.D., professor, Department of Pathology, Brigham and Women's Hospital

Hugh Auchincloss, M.D., associate professor of surgery, Harvard Medical School

K. Frank Austen, M.D., director, Inflammation and Allergic Disease Research Section, Brigham and Women's Hospital

Jeffrey Bluestone, Ph.D., professor, Ben May Institute of Cancer Research, University of Chicago

Charles Carpenter, M.D., professor, Department of Medicine, Brigham and Women's Hospital

Leonard Chess, M.D., professor, Department of Medicine, Columbia University

Joseph Davie, M.D., Ph.D., vice president, Department of Research, Biogen, Inc.

C. Garrison Fathman, M.D., professor, Department of Medicine, Stanford University

Maureen Howard, Ph.D., vice president, research, Anergen, Inc.

Jean-Pierre Kinet, M.D., professor, Beth Israel Deaconess Medical Center, Harvard Medical School

Allan Kirk, M.D., Ph.D., senior investigator, Naval Medical Research Institute

Lee Nadler, M.D., professor, Department of Medicine, Dana-Farber Cancer Institute

Megan Sykes, M.D., associate professor, Transplantation Biology Research Center, Massachusetts General Hospital

Laurence Turka, M.D., associate professor, University of Pennsylvania

NIH Is Publishing New Autoimmunity Initiatives

In NIAID's appropriations language, Congress requested that NIH spend $30 million for new research on autoimmunity and autoimmune diseases.

In January, Dr. Varmus approved the plan he developed with the Institute directors to expand research in these fields.

The monies will be spent on the new initiatives listed below and by supplementing some existing initiatives.

Look for these initiatives soon in the *NIH Guide*.

NIH Autoimmunity Research Initiatives, Primary Sponsoring Institute, and Mechanism*

Environment/Infection/Gene Interaction in Autoimmunity, NIEHS (R21)

New Imaging Technologies for Autoimmune Disease, NIAID (R01)

Genetic Bases and Molecular Pathways to Target Organ Involvement in Autoimmune Disease, NIAMS (R01)

Genetics of Multiple Autoimmune Disease – Registry and Repository, NIAID (N01)

Stem Cell Transplantation for the Treatment of Autoimmune Diseases, NIAID (N01)

Collaborative Network for Clinical Research on Immune Tolerance: Implementation of Autoimmune Disease, NIAID (N01)

High Throughput Screens for Immunological Phenotyping of Mouse Mutants, NIAID (R21)

Non-Human Primate Models of Transplantation Tolerance, NIAID (U19)

Pilot/Feasibility Trials of Innovative Therapies for Rheumatic and Skin Diseases, NIAMS (N01)

Human Islet Transplantation into Humans, NIDDK (R01)

*R = research project grant, P = center, U = cooperative agreement, N = contract, BAA = broad agency agreement

NIAID Celebrates 50th Anniversary

On November 19, NIAID celebrated its fiftieth anniversary with a day-long scientific symposium, Cutting-Edge Science and the History That Led to It.

Opening the sessions for the symposium, Dr. Fauci touched on some of the outstanding accomplishments of NIAID scientists and grantees, providing a historical perspective.

Although the Institute was created in 1948, it actually traces its roots back to a small laboratory established in 1887 at the Marine Hospital on Staten Island, NY.

This facility responded to the threat of cholera and other infectious diseases brought to this country by the large influx of immigrants of that era.

It was headed by Dr. Joseph J. Kinyoun, a young medical officer with the Marine Hospital Service, who had learned about the new science of bacteriology in Europe.

Upon returning home, he set up one of the first bacteriologic laboratories, eventually isolating the cholera organism from immigrants in New York.

Dr. Kinyoun's Laboratory of Hygiene was renamed the

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NIAID Celebrates 50th Anniversary—*continued from page 14*

Hygienic Laboratory in 1891 and moved to Washington, DC, where Congress authorized it to investigate infectious diseases and other public health problems.

NIAID's predecessor, the National Microbiological Institute, was established in 1948 when the then-National Institute of Health was divided into several institutes. NMI was renamed NIAID in 1955.

Since then, the Institute's annual budget has grown to about $1.6 billion, supporting 30 Nobel Prize winners, including NIH director, Dr. Harold Varmus.

As Dr. Fauci told Council, "Institute research during the past 50 years has made an extraordinary impact on allergy, immunology, and infectious diseases. It is clear that our mission is more important than ever as infectious diseases remain the leading cause of death in the world and the third leading cause in the U.S."

For an agenda of the special day, go to **http://www.niaid.nih.gov/final/video.htm**.

And visit the Institute's anniversary web page at **http://www.niaid.nih.gov/final/index.htm**, featuring articles on medical progress, Institute history, and a list of NIAID directors.

Balancing the Budget FY 1999—*continued from page 1*

decisions. For the complete article, please see the September 1998 Council newsletter issue of *Council News* in the newsletter section of our web site at **http://www.niaid.nih.gov/ncn/news.htm.**

NIAID Financial Management Plan

- Payline at 20.0 for all research project grants, targeting a success rate of about 42 percent.
- Programmatic adjustments average 7 percent according to percentile score, as follows:

0.0 to 4.0 percentile	5 percent reduction
4.1 to 8.0 percentile	7 percent reduction
8.1 and higher percentile	9 percent reduction

- Recompeting grants (expiring grants for which the PI is again requesting funds) capped at 20 percent more than the previous award.
- Selective pay pool of $9 million to pay grants beyond the payline that are approved by Council.
- $15 million for bridge awards.

HIV Vaccine Program—*continued from page 3*

Vaccine Design and Development Teams initiative funds groups of academic and private sector scientists to conduct applied research.

Built into the contract is a great deal of flexibility regarding the stage of the research; i.e., the contract is designed to kick in at virtually any step of the development process to move a product forward.

For its three objectives, the HIV Vaccine Production contract will provide for scale-up and production of vaccine candidates, preclinical animal testing, and assembly of all information needed for submitting an IND to FDA.

These contracts complement NIAID's existing basic and preclinical vaccine research grant programs: Innovation Grant Program, HIV Vaccine Research and Design Program (HIVRAD), and the Integrated Preclinical/Clinical AIDS Vaccine Development Program (IPCAVD).

For more information on NIAID's HIV vaccine programs and initiatives, go to the DAIDS vaccine web site at **http://www.niaid.nih.gov/daids/vaccine/default.htm**.

NIAID *Council News*

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